Remarks

Upon entry of this amendment, claims 29-32, 51-55, 64, 74-78, 97-101, 110, and 120-123 will be pending in the above-captioned application. Claims 33-50, 56-63, 65-73, 79-96, 102-109, 111-119, and 124-128 have been withdrawn from consideration by the Examiner.

Claims 29, 51, 75, and 97 have been amended to recite that the polynucleotide fragments of these claims are either at least 30 or 50 contiguous nucleotides in length. Moreover, claims 75 and 97 have been amended to recite that the antibody or portion thereof that specifically binds to or is produced by immunizing an animal with either a protein whose sequence consists of the amino acid sequence of the polypeptide encoded by the complete HSATU68 polynucleotide contained in ATCC Deposit Number 97334 or a protein fragment that is encoded by a polynucleotide fragment of the complete HSATU68 polynucleotide contained in ATCC Deposit Number 97334. Support for these amendments are found throughout the specification as filed. Applicant further notes that these amendments do not affect the scope of the claims.

Accordingly, no new matter has been introduced and entry of this amendment is respectfully solicited.

Applicant thanks the Examiner for the telephone interview of May 30, 2003 in which counsel for Applicant reiterated that the Examiner had not considered Reference A1 (Marchese et al) cited on the Information Disclosure Statement submitted July 10, 1998; the Examiner indicated that this reference would be considered. *See*, Paper No. 22. Counsel for Applicant further discussed the utility of the present invention and submitted post-filing date data in a Supplemental Information Disclosure Statement, submitted May 30, 2003, to support Applicant's assertion of utility. Applicant further addresses these issues and traverses the Examiner's rejection under 35 U.S.C. § 101 for lack of utility in Section II below.

Applicant further thanks the Examiner for entering the amendment to the sequence listing and amendment of the sequence errors in the specification as discussed in Paper No. 20, submitted March 18, 2002.

Finally, Applicant notes that there is an inconsistency between the Official Action and form PTO-326 regarding the finality of the instant action. As there are newly raised

rejections and the action itself does not mention any finality, Applicant presumes that the instant action is non-final.

I. Restriction

Pursuant to Paper No. 23, mailed July 21, 2003, the Examiner has maintained the restriction between Groups 1-13, as defined by the Examiner in Paper No. 12, mailed March 28, 2001. In addition, the Examiner has also maintained the further restriction of Groups 14-18, as defined by the Examiner in Paper No. 17, mailed December 17, 2001, which fall within provisionally elected Group III. More particularly, the Examiner contends that Groups 1-18, as cast by the Examiner, do not share a same or corresponding special technical feature, and thus, are not a single inventive concept as defined under PCT Rule 13.1. Paper No. 23, page 2, paragraph 4.

The Examiner has further classified newly added claims 124-126 in Groups 15-17, and held them withdrawn based on the alleged constructive election of Group 3 by original presentation. As discussed in the response filed March 18, 2002, all of claims 29-120 were submitted contemporaneously, prior to the first action on the merits. Accordingly, it is improper to hold Group 3 constructively elected over Groups 14-18.

A. Marchese et al.

The Examiner has asserted that claim 1 of Group 1 as cast by the Examiner "lacks the special technical feature because it is anticipated by Marchese *et al.* (Genomics, 1995). Applicants respectfully disagree and traverse.

Preliminarily, Applicant notes that PCT Rule 13.2 defines a "special technical feature" as "those technical features that define a contribution which each of the claimed inventions, considered as whole, makes over the prior art." Thus, one aspect of a special technical feature is that the feature makes the invention novel over the prior art. Applicant submits that the instant invention indeed has a special technical feature, i.e., the structure of the DNA, and that, contrary to the Examiner's allegation, this special technical feature is novel over Marchese *et al.*

Although Applicant notes that the Examiner has not made a formal anticipation rejection under 35 U.S.C. § 102, Applicant will address the Examiner's allegation of anticipation as the basis for the Examiner's contention that there is no special technical feature, although Applicant respectfully asserts that this equally addresses any issue under

35 U.S.C. §102. The M.P.E.P clearly sets forth in § 2128.02 at 2100-68 that the effective date of a journal article or publication as an anticipatory reference is not the date the reference was mailed, nor the date that it was received by the publisher, but rather the date in which the publication is received by a member of the public. In the instant case, although the Marchese reference was received by the publisher on April 21, 1995 and accepted for publication on June 27, 1995, on information and belief, the publication was not mailed to the public until September 29, 1995. Thus, the earliest date that a member of the public could have received the Marchese reference, i.e., its effective date, was after the September 29, 1995 mailing date.

The M.P.E.P. further sets forth that if the cited reference's effective date is less than one year prior the applicant's filing date, an applicant can overcome anticipation by "swearing behind" the reference using an affidavit under 37 C.F.R. § 1.131. (See, M.P.E.P. § 2133 at 2100-74). As discussed in M.P.E.P § 715.02 at 700-205,

> [t]he 37 CFR 1.131 affidavit or declaration must establish possession of either the whole invention claimed or something falling within the claim (such as a species of a claimed genus), in the sense that the claim as a whole reads on it. *In re. Tanczyn*, 347 F.2d 830, 146 USPQ 298 (CCPA 1965).

Moreover, if the differences between the cited reference and the invention render the invention obvious over the reference, the Rule 1.131 reference is required to show no more than the reference shows. (*Id.*, at 700-205).

Applicant asserts that he was in possession of the polynucleotide sequence of claim 1 prior to the publication date of the Marchese reference. To corroborate this assertion, Applicant has submitted herewith an executed Declaration of the sole inventor of the present invention under 37 C.F.R. § 1.131, Yi Li, which demonstrates possession of the claimed invention prior to the September 29, 1995 mailing date of the publication. Applicant demonstrates that he was in possession of the nucleotide sequence of clone HSATU68 disclosed in original Figures 1A-1C of the instant application, prior to September 1995. Applicant additionally demonstrates that this nucleotide sequence had been determined prior to September 1995, and that this determination occurred at Human Genome Sciences, which is located in the United States.

Applicant notes that, as discussed in Paper No. 20 submitted March 18, 2002, resequencing of the HSATU68 clone deposited with the ATCC revealed an obvious

sequencing error in original Figures 1A-1D which was subsequently corrected in Paper No. 20 and supported by the Declaration of Melanie Lenhart under 37 C.F.R. § 1.132. (*See*, Paper No. 20, page 4, section I). Applicant further notes that the Examiner has accepted the amendment of the sequence disclosed in Figures 1A-1D. (*See*, Paper No. 23, page 4, section 6). Thus, Applicant respectfully asserts that the showing in the Rule 131 declaration is sufficient to antedate the Marchese reference and support Applicant's assertion that the special technical feature of the instant invention is novel. Additionally, although the Examiner has not made a formal rejection under 35 U.S.C. § 102, Applicant respectfully asserts that the showing made above precludes such a rejection based on Marchese *et al.*

B. Groups 1-18 Share a Special Technical Feature

The Examiner has further restricted the invention into Groups 1-18 under PCT Rule 13.1 because the groups allegedly "do not share the same or corresponding special technical feature with Group 1." (*See*, Paper No. 23, page 4, section 5, paragraph 7). Applicant respectfully disagrees and traverses.

As noted in Paper No. 14, submitted September 27, 2001, Groups 1 and 2 are so linked as to form a single general inventive concept under PCT Rule 13.1 and should be examined together. Moreover, Applicant reiterates that M.P.E.P. Appendix AI (the PCT Administrative Instructions) explicitly recognizes that unity of invention exists between a protein and the DNA sequence encoding that protein. (*See*, Paper No. 14, page 18, first full paragraph. *See also*, M.P.E.P. Appendix AI, Example 17, at AI-60-61). Applicant further submits that Groups 3-18 also share the same underlying special technical feature of Groups 1 and 2, namely, the structure of the DNA sequence. For instance, the structure of the DNA sequence defines the amino acid sequence (as set forth in Example 17 of the PCT Administrative Instructions), which in turn is used to generate antibodies and used in the methods of treating and diagnosing associated disease conditions. Thus, Applicant asserts that, using the reasoning set forth in the PCT Administrative Instructions, Groups 1-18 should be properly examined together.

Moreover, Applicant maintains that the Examiner has improperly restricted Groups 14-18 under PCT Rule 13.1. Applicant has provisionally elected Group 3, as cast by the Examiner in Paper No. 12. (See, Paper No. 14, page 17, section III, paragraph 2). Thus, Applicant asserts that the proper comparison for determination of a special technical

feature must be between Groups 14-18 and Group 3 and not, as the Examiner contends, between Groups 14-18 and Group 1. Using this comparison, Applicants note that the special technical feature of Group 3 are novel antibodies that specifically bind the polypeptides of SEQ ID NO:2 as encoded by the polynucleotides of SEQ ID NO:1 or contained in the HSATU68 polynucleotide sequence of ATCC Deposit No. 97334. Applicant asserts that Groups 14-18 are directed to specific forms of antibodies of Group 3 and thus, share the same special technical feature as Group 3. Therefore, Groups 3 and Groups 14-18 clearly form a single general inventive concept under PCT Rule 13.1. Moreover, PCT Rule 13.4 sets forth that

> it shall be permitted to include in the same international application a reasonable number of dependent claims, *claiming specific forms of the invention claimed in an independent claim*, even where the features of any dependent claim could be considered as constituting in themselves an invention.

(*See*, M.P.E.P. Appendix T, at T-48, emphasis added). Thus, PCT Rule 13.4 provides further evidence that Groups 3 and 14-18 should be considered and examined together. Accordingly, Applicant respectfully requests the Examiner to withdraw the restriction under PCT Rule 13.1.

C. Restriction is Improper Even Under 35 U.S.C. § 121

The Examiner has found Applicant's arguments unpersuasive as presented in Paper No. 20 that even if the restriction was made under 35 U.S.C. § 121 because the subject matter presented of Groups 3 and 14-18 do not present a serious search burden. More particularly, the Examiner has stated that 'the search burden is not a specific issue under lack of unity of invention." (*See*, Paper No. 23, page 3, paragraph 4). Applicants assert that the Examiner's restriction of Groups 3 and 14-18 would even be improper under 35 U.S.C. § 121 because, regardless of the separate classification of these Groups, restriction still remains inconsistent with the policy regarding linking claims.

As discussed in Paper No. 20 at page 10, first paragraph, M.P.E.P. § 809 clearly sets forth that

> linking claims must be examined with the invention elected, and should any linking claim be allowed, the restriction requirement must be withdrawn. Any claim(s) directed to the nonelected invention(s), previously withdrawn from consideration, *which depends from or includes all the limitations* of the allowable linking claim must be rejoined and will be fully examined for patentability.

(Emphasis added). The claims encompassed by Group 3 are linking claims to the claims of Groups 14-18. Moreover, the claims of Groups 14-18 encompass subject matter that depends from the subject matter of the claims of Group 3. Thus, according to M.P.E.P. § 809, these claims should be examined together.

For the reasons stated above, the claims of the invention contain a single inventive concept under PCT Rule 13.1 and 13.2 because they share a novel special technical feature. Moreover, the claims of Groups 14-18 are dependent from and contain all of the limitations of the claims of Group 3; therefore, the claims of Group 3 are linking claims of the claims Group 14-18. Thus, the restriction of the claims into Groups 14-18 is improper under both the PCT rules and under 35 U.S.C. § 121. Accordingly, Applicant respectfully requests the Examiner to reconsider and withdraw the restriction, and that the claims of Groups 14-18 be examined with the pending claims of Group 3.

II. Utility Rejections under 35 U.S.C. § 101

The Examiner has rejected claims 29-32, 51-55, 64, 74-78, 97-101, 120-123, and 127-128 under 35 U.S.C. § 101 for alleged lack of utility. More particularly, the Examiner contends that

> [t]he lack of knowledge of the ligand and the function of HSATU68 G-protein coupled receptor does not provide a substantial utility because without function a nexus to the function and disease does not exist.

Paper No. 23, page 6, first paragraph.

Applicants respectfully disagree and traverse this rejection.

To support a utility rejection based on an alleged lack of specific or substantial utility, the Utility Guidelines mandate that a *prima facie* showing must be made by the Examiner and contain the following elements: (1) an explanation that clearly sets forth the reasoning used in concluding that the asserted utility for the claimed invention is not both specific and substantial nor well-established; (2) support for factual findings relied upon in reaching this conclusion (be they documentary or as an explanation of the scientific basis for the factual conclusions); and (3) an evaluation of all relevant evidence of record, including utilities taught in the closest prior art. (*See*, M.P.E.P. § 2107, page 2100-30).

Applicant respectfully asserts that the Examiner has not met the burden of a *prima facie* showing. The Examiner's argument rests merely on the assertion that because the

ligand of the instant receptor protein was not known at the time of filing, that the function of the protein is not known; and therefore, the invention lacks utility. However, Applicant contends that the Examiner has applied an improper standard for rejecting the claims for alleged lack of utility.

In particular, Applicant asserts that a description of the ligand or mechanism by which the receptor functions is unnecessary. Indeed, it is well established that an applicant is not required to set forth the mechanisms through which the invention functions, nor is the applicant required to even know how or why an invention works. *See e.g., Newman v. Quigg*, 11 U.S.P.Q.2d 1340, 1345 (Fed. Cir. 1989); *Diamond Rubber Co. v. Consolidated Rubber Tire Co.*, 220 U.S. 428, 435-36, 55 L. Ed. 527, 31 S. Ct. 444 (1911); *Fromson v. Advance Offset Plate Inc.*, 720 F.2d 1565, 1570, 219 U.S.P.Q. (BNA) 1137, 1140 (Fed.Cir. 1983). As one district court has stated, "It is clear that patentability is not barred by the failure of the inventors to understand the scientific principle or mechanism on which the claimed invention is based, so long as the method and operative result of the invention are correctly described." *Congoleum Indus. v. Armstrong Cork Co.*, 339 F. Supp. 1036, 1057-1058 (E.D. Pa. 1972). Moreover, the United States Court of Appeals for the Federal Circuit explicitly affirmed "[t]he PTO is not a guarantor of scientific theory and... it is not the province of the PTO to ascertain the scientific explanation." *In Re Newman*, 782 F.2d 971, 974 (Fed. Cir 1986).

Thus, the proper legal standard to judge utility does not rest upon whether the function or mechanism of action, i.e., the ligand, is known. Rather, the standard for supporting a utility rejection is whether one of skill in the art, upon reading the entire specification, would find the asserted utilities for the claimed invention an "inherently unbelievable undertaking or involve implausible scientific principles". *Nelson v. Bowler*, 626 F.2d 853, 857 (C.C.P.A. 1980).

Contrary to the Examiner's allegations, Applicant has set forth in the specification statements that clearly provide the specific, substantial, and credible asserted utility that the Examiner contends is lacking. For example, the specification discloses that the polypeptides of the invention are a member of the human G-protein coupled 7-transmembrane chemokine receptor family that shares significant homology with human interleukin-8 receptor, a C-X-C subfamily member. *See, e.g.*, specification at page 1, lines 5-11; at page 3, lines 11-25; at page 6, lines 24-26; at page 7, lines 23-26; and at Figure 2.

The specification further discloses that these polypeptides have uses, for example, to make and screen agonists, such antibodies, which specifically bind to the receptor of the invention. *See, e.g.*, specification at page 30, lines 29-31. Moreover, the specification clearly sets forth an operative result of the invention, in that compounds that bind to and activate the polypeptides of the invention, i.e., antibodies, are useful in the diagnosis and/or treatment of tumors, such as leukemia. *See, e.g.*, specification at page 5, lines 8-14; and at page 22, lines 3-7. Thus, Applicants submit that the assertion that the antibodies of the invention are useful, for example, in the diagnosis and/or treatment of tumors, such as leukemia, is specific and substantial to satisfy the requirements of 35 U.S.C. § 101.

In corroboration of Applicant's assertions that the antibodies of the present invention are useful, for example, in the diagnosis and/or treatment of tumors, such as leukemia, Applicants respectfully direct the Examiner's attention to the post-filing reference, Lasagni *et al.*, "An alternatively spliced variant of CXCR3 mediates the inhibition of endothelial cell growth induced by IP-10, Mig, and I-TAC, and acts a functional receptor for Platelet Factor 4," *J. Exp. Med.* 197(11):1537-1549 (2003) (Reference CP on the Supplemental Information Disclosure Statement submitted herein). This publication discloses a splice variant of chemokine receptor CXCR3, CXCR3-B, that is identical to CXCR3 except for an additional 52 amino acids at the N-terminal extracellular domain. *See*, page 1539, column 2. Applicant notes that the disclosed splice variant also has 100% identity with the polypeptide disclosed in SEQ ID NO:2 of the present invention. *See*, alignment attached hereto as Exhibit 1.

Lasagni *et al.* discloses that CXCR3B, like CXCR3, binds to chemokines IP-10/CXCL10, MIG/CXCL9 and I-TAC/CXCL11. In addition, CXCR3B also binds platelet factor 4/CXCL4. *See*, page 1540, column 2 to page 1541, column 1. As discussed by the authors, these chemokines have been shown to be involved in the anti-angiogenic and necrotic activities in tumors and are useful, therefore, in the treatment of tumors. See, page 1537, column 2. Thus, because the ligands signal through the CXCR3B receptor, the receptor itself is also useful in the treatment of tumors.

Moreover, overexpression of CXCR3B resulted in a decrease in proliferation rate compared to mock transfectants. In particular, the authors show that this low proliferation rate is associated with a high degree of apoptotic cell death. *See*, page 1541, second column; and page 1542, Figure 3a. In addition, upon binding of CXCR3B, CXCL4 and

CXCL10 significantly upregulated expression of cell cycle regulatory molecule, p21, independently of p53. *See*, page 1543, second column. The authors further discuss the importance of this upregulation through binding of CXCR3B, "because a p53-independent up-regulation of p21 levels is responsible for the antiangiogenic property of CXCL4." Page 1547, first column.

The authors further show that the ligands signal through the CXCR3B receptor via adenylyl cyclase pathway. *See*, page 1543, first column. The authors note that the increase of adenylyl cyclase in response to CXCL10 and CXCL4 has been previously associated with inhibition of cellular proliferation, in particular, in endothelial cells. *See*, page 1547, first column. Moreover, antibodies specific to CXCR3B reacted with endothelial cells from neoplastic tissues, but not with those from their normal counterparts. See, page 1545, second column to page 1546, first column. Thus, the evidence presented as a whole indicates that CXCR3B plays a role in the inhibition of angiogenesis associated with tumor formation. Accordingly, this data supports Applicant's assertion that the antibodies of the present invention are useful, for example, in the diagnosis and/or treatment of tumors, such as leukemia.

Applicant notes that post-filing date scientific papers may be used to corroborate Applicant's asserted utility. Legal precedent for the use of post-filing date references in this manner can be found in *In re Brana*, where the courts stated:

> The Kluge declaration, though dated after applicants' filing date, can be used to substantiate any doubts as to the asserted utility since this pertains to the accuracy of a statement already in the specification. *In re Marzocchi,* 439 F.2d at 224 n.4, 169 U.S.P.Q. (BNA) at 370 n.4.
>
> 51 F.3d 1560, 1567, 34 U.S.P.Q.2D (BNA) 1436 (Fed. Cir. 1995).

Further, the requirement for further research does not preclude meeting the requirements of 35 U.S.C. § 101. Applicant asserts that there is no need to prove that a correlation exists between a particular activity and an asserted use of a compound as a matter of statistical certainty or provide actual evidence of success in human where such a utility is asserted. *See* M.P.E.P. § 2107.02 at 2100-[33-34]. All that is required is there be a reasonable correlation between the biological activity and the asserted utility. *See Nelson v. Bowler*, 626 F.2d 853, 857 (C.C.P.A. 1980), emphasis added. Moreover, the Federal Circuit has held that "[u]sefulness in patent law, and in particular in the context of

pharmaceutical inventions, necessarily includes the expectation of further research and development. The stage at which an invention in this field becomes useful is well before it is ready to be administered to humans" *In re Brana*, 51 F.3d 1560, 1566, 34 USPQ2d 1436, 1441 (Fed. Cir. 1995).

As a final point, Applicant refers the Examiner to the ruling in *Raytheon v. Roper*, 724 F.2d 951 (Fed. Cir. 1983). In this case, the district court found that claims 2-7 of the patent at issue were invalid for lack of utility, and also found that these same claims had been infringed. The Federal Circuit affirmed the holding of infringement, but concluded that the lower court's holding of invalidity due to lack of utility was clearly erroneous because the finding of infringement compelled the conclusion that the claims accomplished at lease one of the asserted utilities. *Id.* Consequently, "[i]f a party has made, sold, or used a properly claimed device . . . proof of that device's utility is thereby established." *Id.*

In this light, the Examiner's attention is respectfully directed to the post-filing date R & D Systems Technical Data Sheet for Monoclonal Anti-Human CXCR3 Antibody, (catalog number MAB160, cited as Reference CK in Applicant's Information Disclosure Statement of May 30, 2003). On information and belief, R & D Systems began offering this antibody for sale in December of 1998. Moreover, the technical data sheet lists as its clone id 49801, which has been shown by Lasagni *et al.* to bind to a common region of both CXCR3 and the splice variant, CXCR3, and neutralize the functional activity of both receptors. *See*, page 1540, column 1; and page 1546, column 1. Accordingly, Applicant respectfully submits that the commercial marketing and the subsequent public use of the claimed invention is conclusive evidence of a "real world" use.

Thus, Applicant has herewith provided evidence of the logical scientific reasoning behind the assertions that the antibodies of the invention have uses, for example, in the diagnosis and/or treatment of tumors, such as leukemia. Applicant contends that based on the totality of the evidence, a skilled artisan would find the statements of utility contained in the specification to be specific, substantial, and credible. Accordingly, Applicant respectfully requests that the rejection under 35 U.S.C. § 101 be reconsidered and withdrawn.

The Examiner has also rejected claims 29-32, 51-55, 64, 74-78, 97-101, 110, 120-123, and 127-128 under 35 U.S.C. § 112, first paragraph, for alleged lack of enablement.

In view of the reasons discussed above in response to the rejection under 35 U.S.C. § 101, the claimed invention is supported by a credible, specific, and substantial utility. The Examiner "should not impose a 35 U.S.C. § 112, first paragraph, rejection grounded on a 'lack of utility' basis unless a 35 U.S.C. § 101 rejection is proper." M.P.E.P. § 2107(IV). Therefore, since the claimed invention complies with the utility requirements of 35 U.S.C. § 101, Applicant respectfully requests that the rejection under 35 U.S.C. § 112, first paragraph, be reconsidered and withdrawn.

III. Indefiniteness Rejections under 35 U.S.C. § 112, Second Paragraph

A. Claims 29-32, 51-55, 64, 74-78, 97-101, 110, 120-123, and 127-128

The Examiner has rejected claims 29-32, 51-55, 64, 74-78, 97-101, 110, 120-123, and 127-128 under 35 U.S.C. § 112, second paragraph for alleged indefiniteness. More particularly, the Examiner contends that the term "specifically binds" is ambiguous because

> [t]he degree of binding is determined by the binding conditions of the assay and metes and bounds of when something binds specifically cannot be determined without the binding assay limitations compared with the standard control non-specific binding assay.

Paper No. 23, page 8, section 8, paragraph 2.

Applicant respectfully disagrees and traverse this rejection.

Applicant respectfully submits that the term "specifically" is not indefinite when considered in the context of M.P.E.P. § 2173.01 at 2100-194 which outlines the proper legal standard for examining 35 U.S.C. § 112, second paragraph, as follows:

> The essential inquiry pertaining to this [35 U.S.C. § 112, second paragraph] requirement is whether the claims set out and circumscribe a particular subject matter with a reasonable degree of clarity and particularity. Definiteness of claim language must be analyzed, not in a vacuum, but in light of:
>
> a. The content of the particular application disclosure;
> b. The teachings in the prior art; and
> c. The claim interpretation that would be given by one possessing the ordinary skill in the pertinent art at the time the invention was made.

As an initial matter, Applicant provides a definition of the phrase "specifically binds" from a 1991 textbook, Immunology: a Synthesis, second edition, Golub and Green, pp 23-27, attached hereto as Exhibit 2 (emphasis added):

> *Specificity* is defined as the ability of antibodies produced in response to an antigen to react with that antigen and not with others....Antibody molecules can exhibit great *specificity*, but there are cross-reactions – cases in which antibody to antigen A also reacts with antigen B. This can be due to the presence of the same molecular configuration, or antigenic determinant, on the two antigens....Antigenic determinant are also called epitopes.

Applicant submits that the phrase "specifically binds," as defined above, is a term of art which is routinely used, recognized, and understood by those of ordinary skill in the antibody arts.

For example, routine assays for identifying a "specific" antibody were available as of the priority date of the present application. *Current Protocols in Immunology*, a common laboratory handbook, provides three such assays: (1) Indirect ELISA to Detect *Specific* Antibodies; (2) Double Antibody-Sandwich ELISA to Detect *Specific* Antibodies; and (3) Double-Immunodiffusion Assay for Detecting *Specific* Antibodies (*see, e.g.,* Current Protocols in Immunology ed. Coligan *et al.* Vol. 2, Sections 2.1.1-2.1.20 and 2.3.1-2.3.3 (1991), attached hereto as Exhibit 3 (emphasis added). These assays could readily be used by one of ordinary skill in the art to determine, without undue experimentation, if antibodies specifically bind to a polypeptide.

Furthermore, the 1994 Boehringer Mannheim Biochemicals Catalog (the "1994 Catalog"), uses the term "specificity" to describe one of the many features of the antibodies which are offered for sale. For example, the catalog lists an Anti-Mac-1 (macrophage associated antigen) (clone M1/70) antibody and describes it under the heading "Specificity and Notes":

> The antibody *specifically* reacts with native mouse and human Mac-1 (complement receptor type 3; Ly-40) antigen and precipitates two chains, 170kD (CD11b) and 95kD (CD18).

Boehringer Mannheim Biochemicals, Inc. 1994 Catalog, page 260, enclosed herewith as part of Exhibit 4 (emphasis added). As a further example, an Anti-L-CAM/Uvomorulin (clone 6F9) antibody is described:

> The antibody *specifically* recognizes the 120 kD and the 80 kD band of L-CAM/Uvomorulin (Arc-1 E-cadherin cell-CAM 120/80) in man and rabbit. L-CAM/Uvomorulin staining is confined to the lateral border of epithelial cells and, within the intestine, shows more intense concentrations in the area of the junctional complex. As a positive control, the cell line MCF-7 can be used.

Id. at page 280, attached hereto as part of Exhibit 5 (emphasis added).

While the 1994 Catalog does not claim that the "specific" antibodies listed bind the desired protein to the exclusion of all other proteins, it would be clear to one of ordinary skill in the art that these antibodies preferentially bind to their target antigen, *i.e.* they are specific and not cross-reactive. Otherwise, the antibodies would not be appropriate for their advertised use (*e.g.*, in the examples cited above, cryosections, Western (protein) blots, immunocytochemistry, or ELISA; and flow cytometry, immunocytochemistry, or immunoprecipitation, as shown on pages 260-261 and 280-281 of Exhibit 6, respectively).

In agreement with the examples given above, Applicant's disclosure clearly contemplates an antibody that specifically binds the polypeptides of the instant invention. For example, the specification, on page 28, second paragraph recites that

> [a]n ELISA assay initially comprises preparing an antibody specific to antigens of the G-protein chemokine receptor polypeptides, preferably a monoclonal antibody.

(Emphasis added).

Thus, Applicant submits that because of (1) the use of the term "specific" in the prior art to describe the binding of antibody to antigen in textbooks, research manuals, and catalogs; and (2) the content of Applicants disclosure, those of ordinary skill in the antibody arts would have recognized and understood the use of the term "specifically binds" in the claims at issue. Accordingly, Applicants respectfully request the Examiner to reconsider and withdraw the rejection of claims 29-32, 51-55, 64, 74-78, 97-101, 110, 120-123, and 127-128 under 35 U.S.C. § 112, second paragraph for lack of definiteness.

B. Claims 75-78

The Examiner has also rejected claims 75-78 under 35 U.S.C. § 112, second paragraph for alleged indefiniteness. In particular, the Examiner asserts that the term "HSATU68 polypeptide coding region" is indefinite and ambiguous because

> [t]he term "HSATU68 polypeptide does not provide a specific structure of the polypeptide and can encompass a fragment of two amino acids which is encoded by ATCC deposit 97344.

Paper No. 23, page 8, section 8, paragraph 3.

Applicant respectfully disagrees and asserts that the language of previous claims 75-78 clearly sets forth the metes and bounds of the subject matter claimed as originally presented. However, Applicant has amended claim 75 without prejudice or disclaimer to refer to "the complete HSATU68 polynucleotide", thus obviating the instant rejection. Accordingly, Applicant respectfully requests the Examiner to reconsider and withdraw this rejection under 35 U.S.C. §112, second paragraph for lack of definiteness.

IV. Written Description Rejections under 35 U.S.C. § 112, First Paragraph

The Examiner has rejected claims 29-32, 51-55, 64, 74-78, 97-101, 110, 120-123, and 127-128 under 35 U.S.C. § 112, first paragraph for alleged lack of written description. More particularly, the Examiner asserts that:

> [t]he claims encompass antibody which bind variants whose structure is not known or other variant proteins with different function from SEQ ID NO:2 taught in the specification because the term "comprising" encompass structures which is not part of SEQ ID NO:2

Paper No. 23, section 9, paragraph 2.

Applicant respectfully disagrees and assert that the claims at issue are adequately described by the specification as filed. Moreover, claims 29, 51, 75, and 97 have been amended to recite that the polynucleotide is at least 30 or 50 contiguous nucleotides in length of either SEQ ID NO:2 or of the complete HSATU68 polynucleotide encoded by ATCC Deposit No. 97334. Thus, contrary to the Examiner's argument and for the reasons set forth below, Applicant contends that the pending claims are fully described by the instant application.

The test for the written description requirement is whether one skilled in the art could reasonably conclude that the inventor has possession of the claimed invention in the specification as filed. *See* M.P.E.P. § 2163(I) at 2100-15, and *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563, 19 USPQ2d 1111, 1116 (Fed. Cir. 1991). In particular, written description is satisfied if the specification allows the skilled artisan "to visualize or recognize the identity

of the members of the genus." *Regents of the University of California v. Eli Lilly & Co.*, 119 F.3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Contrary to the Examiner's arguments, Applicant submits that the specification provides ample written description to enable one of skill in the art to visualize or recognize the identity of the members of the claimed genus. Applicant further submits that the instant application provides precisely that which the Examiner states are the essential feature of the invention, namely, the peptide of SEQ ID NO:2. (*See*, Paper No. 23, page 9, section 9, paragraph 2). Moreover, the specification provides the skilled artisan, for example, with the detailed structure of the polypeptide of the invention, *e.g.*, the amino acid sequence of SEQ ID NO:2. *See*, specification, for example, at page 6, lines 28-31; at page 8, lines 1-9; at page 10, lines 35-38; and at Figures 1A-1D.

In addition to the amino acid sequence common to the polypeptides of the claimed invention (e.g., SEQ ID NO:2), the specification further contemplates polynucleotides that encode fragments of SEQ ID NO:2 or fragments of the complete polynucleotide sequence contained in the ATCC Deposit which are at least 30 or 50 contiguous nucleotides in length. *See* specification, for example, at page 8, lines 17-21; and at page 10. Moreover, the specification describes that such polypeptide fragments may be used as immunogens to produce antibodies thereto. *See*, specification, for example, at page 30, line 29 to page 31, line 26.

Accordingly, one skilled in the art, enlightened by teachings of the present application, could readily envision the antibodies or portions thereof of the invention that bind to the specified polypeptide fragments of SEQ ID NO:2 or the Deposit which are encoded by polynucleotides at least 30 or 50 contiguous nucleotides in length. Indeed, nothing more than what is described in the specification would be required for the skilled artisan to identify every single one of the polypeptides of SEQ ID NO:2 encoded by polynucleotides that are at least 30 or 50 nucleotides in length. Moreover, the skilled artisan can then readily determine using techniques well known within the art whether the antibody or fragment thereof specifically binds such encoded portions of SEQ ID NO:2 or the Deposit. Clearly, such knowledge is well within what is expected of the skilled artisan.

Thus, the instant claims clearly distinguish the boundaries of each claimed genus and identify all of the members of each genus. Accordingly, one skilled in the art would

reasonably conclude that Applicant had possession of the antibodies encompassed by the rejected claims, upon reading the present application as filed.

Accordingly, from reading the specification, the skilled person would immediately recognize that, at the time the specification was filed, the Applicants had "invented what is claimed" (*Vas-Cath*, 935 F.2d at 1563); namely, a genus of antibodies or portions thereof that specifically bind to a protein consisting of a protein fragment of SEQ ID NO:2 encoded by a polynucleotide fragment, wherein said polynucleotide fragment is at least 30 or 50 contiguous nucleotides in length. Therefore, the specification contains an adequate written description of the claimed antibodies.

For all of the above reasons, Applicant respectfully asserts that the specification conveys with reasonable clarity that Applicant was in possession of the claimed invention. Therefore, Applicants submit that the pending claims fully meet the written description requirements of 35 U.S.C. § 112, first paragraph, and respectfully request that the Examiner's rejection of the claims 29-32, 51-55, 64, 74-78, 97-101, 110, 120-123, and 127-128 under 35 U.S.C. § 112, first paragraph, be reconsidered and withdrawn.

V. Enablement Rejection under 35 U.S.C. § 112, First Paragraph

The Examiner has rejected claims 29-32, 51-55, 64, 74-78, 97-101, 110, 120-123, and 127-128 under U.S.C. § 112, first paragraph for alleged lack of enablement. In particular, the Examiner asserts that

> ...the specification does not teach how to use an antibody which binds peptide variant or fragment HSATU68 polypeptide because HSATU68 polypeptide has no ligand which can be used to determine the function for the HSATU68 polypeptide protein.

Paper No. 23, page 10, section 10, paragraph 2.

Applicant respectfully disagrees and assert that the claims at issue are adequately described by the specification as filed. Moreover, claims 29, 51, 75, and 97 have been amended to recite that the polynucleotide is at least 30 or 50 contiguous nucleotides in length of either SEQ ID NO:2 or of the complete HSATU68 polynucleotide contained in ATCC Deposit No. 97334. Thus, contrary to the Examiner's argument and for the reasons set forth below, Applicant contends that the pending claims are fully enabled by the instant application.

Applicant notes that the underlying basis for the Examiner's rejection in section 10 of Paper No. 23 is the assumption that the pending claims encompass variants with a different amino acid sequence from SEQ ID NO:2 due to the "comprising" language in relation to 30 and 50 contiguous nucleotides. However, as noted above, the pending claims, as amended, do not contain the open-ended term "comprising" in relation to 30 or 50 contiguous nucleotides. Rather these claims have been amended to recite that the antibody or fragment thereof specifically binds a protein consisting of a protein fragment of SEQ ID NO:2 that is encoded by a polynucleotide fragment of SEQ ID NO:1 or by the complete HSATU68 polynucleotide, and that the polynucleotide fragment must be at least 30 or 50 contiguous nucleotides in length. Thus, the antibodies encompassed by the pending claims are only required to bind the amino acid sequence of SEQ ID NO:2 or bind a fragment encoded by a polynucleotide of SEQ ID NO:1 or bind the polypeptide encoded by a polynucleotide fragment of the complete HSATU68 polynucleotide contained in the ATCC deposit.

Moreover, Applicant contends that while knowledge of the ligand for the receptor or of the tertiary structure of the receptor is useful information, this knowledge is not necessary to enable the antibodies of the pending claims, particularly when the invention has utility, as discussed above in Section II. All that is required for the pending claims to be fully enabled is that the specification teaches the skilled artisan to make fragments of the amino acid sequence of SEQ ID NO:2 or fragments that are encoded by the polynucleotides of SEQ ID NO:1 or in the ATCC Deposit, generate antibodies, and then screen these antibodies to determine those that specifically bind to the amino acid sequence of SEQ ID NO:2 or a fragment thereof.

Applicant contends that the specification clearly teaches one of skill in the art how to make and isolate polypeptides of SEQ ID NO:2 encoded by polynucleotide fragments of SEQ ID NO:1 or encoded by the HSATU68 polynucleotides contained in ATCC Deposit 97334 which are at least 30 or 50 contiguous nucleotides in length. *See* specification, for example, at page 8, lines 17-21; at page 10; and at Examples 1-3, page 33, line 13 to page 39, line 9. In addition, the specification teaches, for example, at page 28, line 20 to page 29, line 6; and at page 30, line 29 to page 31, line 26 how to make, isolate, and screen for antibodies that specifically bind polypeptides of the invention, including fragments. Thus,

the specification clearly teaches the skilled artisan how to make and use the claimed invention.

For all of the above reasons, Applicant asserts that the specification is fully enabling for the subject matter encompassed by the pending claims. Accordingly, Applicant respectfully requests the Examiner to reconsider and withdraw the rejection of claims 29-32, 51-55, 64, 74-78, 97-101, 110, 120-123, and 127-128 under 35 U.S.C. § 112, first paragraph for lack of enablement.

Conclusion

Applicant respectfully requests that the above-made remarks and amendments be entered and made of record in the file history of the instant application. In view of the foregoing remarks, Applicant believes that this application is now in condition for allowance, and an early notice to that effect is urged. The Examiner is invited to call the undersigned at the phone number provided below if any further action by Applicant would expedite the allowance of this application. If there are any fees due in connection with the filing of this paper, please charge the fees to our Deposit Account No. 08-3425. If a fee is required for an extension of time under 37 C.F.R. § 1.136, such an extension is requested and the fee should also be charged to our Deposit Account.

Dated: December 16, 2003

Respectfully submitted,

By _____

Mark J. Hyman
Registration No.: 46,789
HUMAN GENOME SCIENCES, INC.
9410 Key West Avenue
Rockville, Maryland 20850
(240) 314-1224

KKH/MJH/KC/lcc